

### **Remarks and Arguments**

Applicant respectfully requests reconsideration and submits the following in response to the Office Action mailed September 23, 2004.

#### **Claims amendments**

By this amendment, Applicant has canceled claims 1 - 4 and 17 - 53 without prejudice or disclaimer. Claim 54 has been added to more particularly point out the invention. It incorporates subject matter, from claims 53 as well as claims 1, 3 and 4. Claims 8, 10 and 12 have been amended to depend from claim 54. Applicant submits that no new matter has been added and the claims are amended to more specifically recite that which the Applicant regards as being patentable. Support for the amendments can be found on pages 3-4 of the specification and in the claims as originally filed.

#### **Rejections Under 35 U.S.C. § 102(e)**

Claims 1, 10 and 11 stand rejected under §102(e) over Flower 6,351,663 (hereinafter "Flower '663"). As claims 1 and 53 have been canceled, Applicant respectfully traverses this rejection with respect to new claim 54 and claims 10 and 11, as set forth below.

The Office alleges that Flower '663 anticipates claims 1, 10, and 11, but admits that Flower '663 fails to show explicitly a given blood vessel and a bypass graft as being used on that particular graft (page 3 of the Office Action dated 9/23/2004). New claim 54 recites: "(b) obtaining at least one angiographic image of the at least one blood vessel portion; and (c) evaluating the at least one angiographic image to determine patency of the at least one blood vessel portion, wherein the at least one blood vessel is a coronary artery, wherein the at least one blood vessel portion is a bypass graft." Applicant's submit that claim 54, by the Office's own admission does not recite each and every element of the claim and therefore cannot anticipate claim 54. All other pending claims under consideration depend, either directly or indirectly, on claim 54.

Moreover, Applicants submit that Flower discloses occlusion and destruction of blood vessels for purposes of vessel occlusion, but not for purposes of patency assessment. Flower discloses that ICG can be used to identify blood vessels feeding various abnormalities. (Col. 2, lines 22-25). Injecting ICG, at a certain concentration, into the blood stream with a subsequent introduction of light energy causes the ICG to fluoresce. Images of the fluorescing dye are then captured. (Col. 4, lines 16 - 46). Flower also discloses that the ICG can be excited by energy that will cause the ICG to heat up which, as a result of the increased heat, causes the blood vessel in which the ICG is located to become obstructed. If the blood vessel is feeding a lesion, e.g., a tumor, the stoppage of blood to the tumor may serve to cause the tumor to shrink. (Col. 5, lines 4 - 31). Further, the amount of obstruction can be determined by analyzing angiograms taken after the dye has left the treated vessel. (Col. 5, lines 32 - 39).

In contrast, claim 54 is directed to a method for visualizing, during an invasive surgical procedure on an animal, at least a portion of at least one blood vessel of the animal that is exposed by the procedure. The method comprises administering a fluorescent dye to the animal, obtaining at least one angiographic image of the blood vessel portion and evaluating the at least one angiographic image to determine patency of the at least one blood vessel portion. As recited in claim 54, the blood vessel is a coronary artery, wherein the at least one blood vessel portion is a bypass graft.

In order to anticipate a claim, a reference must recite each and every limitation of the claim. Flower, however, does not disclose evaluating, during a bypass procedure, patency of a bypass graft of a coronary artery, as recited in claim 54. For at least the foregoing reasons, Applicant submits that Flower does not anticipate claim 54 and its dependent claims 10 and 11.

### **Rejections Under 35 U.S.C. § 103**

Claims 2-5, 8, 9 and 53 stand rejected under § 103 as being unpatentable over Flower '663 in view of Collen, U.S. Patent 5,951,980 (hereinafter "Collen"). Applicant submits the following with respect to independent claim 54 and claims 5, 8 and 9.

Applicant submits that the Office has failed to establish a prima facie case of obviousness because there has been no showing, by the Office, of motivation to

combine the teachings of Flower with the teachings of Collen, moreover the cited references do not teach or suggest all of the claim limitations.

Obviousness is a legal conclusion based on factual evidence. Graham v. John Deere Co. 383 US 1, 148 USPQ 459 (1966). The PTO has the burden under 35 U.S.C. §103 to establish a prima facie case of obviousness. In re Plasecki, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-87 (Fed. Cir. 1984). In order to establish a prima facie case of obviousness, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991.) There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art and the knowledge of persons of ordinary skill in the art. In re Rouffet, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-1458 (Fed. Cir. 1998.)

The Examiner has not pointed to any motivation to be found in Flower to motivate one to combine it with the teachings of Collen. Collen is directed to the identification of staphylokinase derivatives with reduced immunogenicity, their identification, production and use in the treatment of arterial thrombosis. (Col. 1, lines 15-18). Collen is directed to various processes for preparing these amino acids. Flower discloses occlusion of arteries in the eye to treat various conditions. Nothing in either reference suggest combining their disclosures to intra-operatively assess the patency of a coronary artery.

The Examiner maintains that Collen teaches the taking of an angiographic image "before and after the invasive procedure." (Office Action, p. 3). But the images suggested by Collen are merely before and after treatment with staphylokinase. They do not record a dynamic event concurrent with surgery. Nor are they performed on a vessel that is exposed by the procedure.

Claim 54 is directed to the method of visualization, **during an invasive surgical procedure**, (emphasis added) and, more specifically, a cardiac by-pass grafting procedure. Collen clearly is referring to angiography **after** a procedure as it is concerned with the long term efficacy of the staphylokinase derivatives. There is no teaching or suggestion of angiography during the invasive procedure to be found in Collen and as recited in independent claim 54.

In order to render obvious that which is recited in Applicant's claim 54, each and every limitation must be found in the cited combination. The Office has already admitted that Flower fails to teach or suggest all of the limitations of claim 54, and Collen does not remedy Flower's deficiencies in that regard. Collen merely refers to angiography in passing, and does not teach or suggest a method for visualizing, during an invasive surgical procedure on an animal, at least a portion of at least one blood vessel of the animal that is exposed by the procedure, as recited by claim 54. The procedure suggested by Collen is post-operative. Column 13, lines 29-30 of Collen state occlusions of less than 120 days duration were treated with staphylokinase. Thus the combined references do not teach or suggest a method for visualizing, during an invasive surgical procedure on an animal, at least a portion of at least one blood vessel of the animal that is exposed by the procedure. Because the cited references do not teach all of the claim limitations, they cannot render the claims obvious.

Lastly, there would be no reasonable expectation that the disclosure of Collen could be successfully combined with Flower to arrive at the instant invention. The disclosure in Flower regarding the eye does not involve the urgency of surgery on a vital organ where images on individual vessels must be obtained and interpreted rapidly. Similarly there would be no immediate urgency associated with the procedure suggested by Collen where the long term effects of treatment are being evaluated. At best, the combination would be obvious to try. Obvious to try, however, is not the standard under 35 U.S.C. § 103. *In re O'Farrell*, 7 U.S.P.Q. 1673, 1680 (Fed. Cir. 1988).

Applicant submits, therefore, that independent claim 54 and its dependent claims 8 and 9 are patentable over the cited combination of references.

Claims 12 and 13 stand rejected under § 103 as being unpatentable over Flower '663 in view of Feiler, U.S. Patent 5,375,603 (hereinafter "Feiler"). Applicant respectfully submits the following in response.

Applicant submits that the Office has failed to establish a prima facie case of obviousness because there has been no showing, by the Office, of motivation to combine the teachings of Flower with the teachings of Feiler.

Feiler is directed to a process for determining the effectiveness of a graft that is positioned during a by-pass grafting procedure. Feiler teaches the use of thermography to identify those areas of an organ, e.g., a heart, that are not receiving a sufficient blood supply. A temperature difference will indicate a diminished blood supply. An infrared sensing device is used to map surface temperatures of the heart to identify areas of inadequate blood flow. (Col. 3, lines 15-18). The heart is perfused with a solution to aid in establishing a temperature difference between areas of the heart receiving sufficient blood supply and those that do not. (Col.5, lines 3-60).

More importantly, Feiler discloses that thermal imaging is successful during open heart surgery. Thus, there would be no motivation to try the fluorescent dye disclosed in Flower with the thermal imaging during heart surgery disclosed in Feiler, as the Office suggests. A skilled artisan reading Feiler would not be motivated to combine its disclosure with that of Flower, because based on the disclosure in Feiler there would be no perceived problem to be solved. Motivation to combine two references requires a perceived problem to be solved. See *Winner v. Wang*, 202 F.3d 1340, 1349, 53 U.S.P.Q.2d 1580, 1587 (Fed. Cir. 2000).

Moreover, there is no reasonable expectation of success in combining the teachings of Flower and Feiler. Flower is directed to identifying specific blood vessels that are candidates for treatment in areas of the body that are reachable by access directly or through a body cavity that permits the introduction of an endoscope. (See Col. 8, lines 42-49.) Feiler, on the other hand, infers that blood is flowing because of the temperature profile but does not specifically identify which blood vessels are supplying the blood. Further, it is inherent in Flower that the heart is beating. Feiler, on the other hand, teaches the use of thermography to assess blood flow by analysis of a heart that has been stopped where mechanical means are provided to cause fluid to flow. This technique of thermal imaging while a heart is stopped, however, would not work with Flower's process. Applicant submits, therefore, that the cited combination is improper and should be withdrawn.

Claim 54 is directed to a method of visualizing that comprises administering a fluorescent dye to the animal, during an invasive surgical procedure, and evaluating patency of a graft.

Applicant submits that the combination of Flower and Feiler does not render obvious that which is recited in Applicant's claim 54. As above, Flower is silent as to determining patency of a graft during an invasive surgical procedure. Feiler relies on temperature differences and images thereof to visualize blood perfusion in an arrested heart.

Applicant respectfully submits that, for at least these reasons, claims 54, 12 and 13 are patentable over the cited combination of references.

Claims 14 and 15 stand rejected under § 103 as being unpatentable over Flower '663 in view of Feiler as applied to claims 12 and 13 and further in view of Alfano, U.S.P. 6,280,386 (hereinafter "Alfano"). The Office alleges Alfano discloses using a CCD camera and an apparatus for enhancing an image obtained from a CCD camera. Applicant responds as follows.

Alfano is directed to applying a contrast agent to a sample to be imaged to create a luminous object. (Abstract). Various contrast agents are disclosed and are chosen based on the specific binding properties that the agent exhibits. As disclosed by Alfano, different contrast agents can be selected which exhibit specific binding properties to different molecules in different organs, e.g., breast, liver and brain. (Col. 5, lines 7-16).

In Alfano, the process includes treating a tissue sample with the contrast agent, illuminating the sample with monochromatic light at a first wavelength and capturing two images at two different wavelengths. A CCD camera is used to capture the images. A difference between the two captured images is obtained to provide an enhanced image signal. (Col. 5, lines 16-36, Fig. 4)

Applicant submits that the Examiner has not established a prima facie case of obviousness as there has been no showing of motivation to combine these references. The combination of Flower and Feiler has been discussed above. Nothing in Alfano cures the defects discussed above regarding the combination of Flower and Feiler. Alfano is directed to staining tissue with a fluorescent agent, capturing images at two

different wavelengths and taking the difference between the two images to obtain a better image for evaluation.

One of ordinary skill in the art would not be motivated to combine these references. Flower identifies specific blood vessels, Feiler is directed to determining general blood perfusion and Alfano is directed to imaging tissue. Flower and Feiler are dynamic applications while the application of the process of Alfano is static. Thus there would be no motivation to combine the static system suggested by Alfano with the dynamic systems suggested by Feiler and Flower.

There would be no reasonable expectation in combining the disclosure of Alfano with that of Feiler and Flower. The staining of Alfano would not work in the application of Flower or Feiler as the stain would attach to all tissue portions and one would be unable to differentiate those areas with good perfusion and those areas without.

For at least the foregoing reasons, Applicant respectfully submits that the cited combination of Flower, Feiler and Alfano does not render obvious that which is recited in claims 5, 14 and 15.

Claim 16 stands rejected under § 103 as being unpatentable over Flower '663 in view of Feiler and Alfano as applied to claims 14 and 15 above and further in view of Borst, 5,927,284 (hereinafter "Borst"). The Office alleges that Borst discloses a method and apparatus for temporarily immobilizing a local area of tissue that shows using an endoscope.

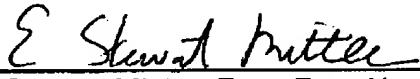
Borst is directed to a device for temporarily immobilizing a local area of tissue on a beating heart to facilitate the placing of a by-pass graft. (Abstract). The device includes suction cups for placement on the heart to reduce the movement from the heart's beating. (Figs. 2A and 2B)

Applicant respectfully submits that while Borst may disclose an endoscope, as does Alfano, Borst does not remedy the deficiencies of Flower, Feiler and Alfano, as submitted above and, therefore, does not render obvious that which is recited in claim 16. Applicants submit that there would be neither motivation, nor reasonable expectation of success in combining Flower with Feiler and adding Borst does nothing to change this.

The amendments to the claims, as set forth herein, including the addition or cancellation of any claims, have been offered to advance this application to issue. None of the amendments made herein should be construed as an admission that the subject matter of the claims, as originally filed, is anticipated by or made obvious in light of any art of record whether considered singularly or in combination. Applicant respectfully reserves the right to pursue the originally filed claims in another co-pending application without being prejudiced by any amendments, including cancellation of claims, made herein.

Applicant believes all claims are in allowable condition. A notice of allowance for this application is earnestly solicited. If the Examiner has any questions regarding this amendment, the Examiner is invited to call Applicant's attorney at the number listed below. The Examiner is hereby authorized to charge any fees or credit any balances under 37 CFR §§1.16 and 1.17 to Deposit Account No. 02-3038

Respectfully submitted,

  
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